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Evaluation of the Effectiveness of Mass Screening for Uterine Cancer in Japan: The Potential Years of Life Lost

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To evaluate the effectiveness of mass screening for uterine cancer in Japan, we compared the changes in the age-adjusted rates of potential years of life lost (PYLL) due to uterine cancer between 1969 and 1972 to 1973 through 1977 between the high coverage-rate (intensively screened) areas and the comparable control areas. The percent reduction in the average age-adjusted rate of PYLL due to uterine cancer and the years of life saved per 100,000 females were greater in the high coverage-rate areas than in the control areas. These results suggested that mass screening programs for uterine cancer contribute to saving years of life.

Introduction

In Japan a mass screening program for uterine cancer was started around 1960. A report published by the Health Service Bureau of the Ministry of Health and Welfare, Fourth Nationwide Survey on Malignant Neoplasms in Japan, carried out in 1979, revealed that mass screening for uterine cancer had been conducted in 98.6% of all the 3278 municipalities in Japan in 1978 (*1*). Under the Health and Medical Services Law for the Elderly, enacted in 1983, all municipalities had an obligation to conduct mass screening programs for uterine cancer. This paper evaluates the effectiveness of mass screening for uterine cancer.

The final goal of cancer control is preventing the disease. An immediate and attainable objective is to prevent or delay cancer mortality and to increase the life expectancy. Mass screening for cancer decreases life shortening caused by cancer because screening permits early cancer detection and prompt curative treatment.

The impact of cancer mortality has usually been presented by the age-adjusted mortality rate. We previously attempted to evaluate the effectiveness of mass screening programs for cancer in the population, using the age-adjusted mortality rates (*2–4*). In this paper, we also attempted to analyze whether or not the mass screening programs for uterine cancer in Japan can contribute to the decrease of the potential years of life lost (PYLL) attributed to uterine cancer. The PYLL tends to emphasize reduction in cancer mortality in younger age groups, while the age-adjusted statistic counts death at younger ages essentially the same as a death at older ages.

Materials and Methods

Potential Years of Life Lost

The PYLL (*5–8*) is calculated based on the expected remaining lifetime of a person at the time of death. We calculated the years of life remaining up until the female life expectancy of the mid-year of the study period in Japan. The PYLL is given by:

$$\text{PYLL} = \sum a_i\, d_i$$

where a_i denotes the remaining years until female life expectancy in Japan in 1973 (mid-year of study period), d_i denotes the number of deaths of age group i.

To compare the PYLLs between the populations with different size and different age structure, age-adjusted rates must be used. Hence,

Age-adjusted rate of PYLL =

$$\sum a_i \left(\frac{N_i}{N}\right)\left(\frac{d_i}{n_i}\right) = \sum a_i\left(\frac{N_i}{N}\right)p_i$$

where N_i denotes the number of persons of age group i of the standard population, Segi-Doll's world population; N denotes the total number of persons of the standard population; n_i denotes the number of persons of

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age group i of the actual population; and p_i denotes the age-specific death rate of age group i from cancer of the uterus in Japan.

Selection of the High Coverage-Rate Areas for Uterine Cancer Mass Screening

Based on the information from the 1979 mass screening published in the Fourth Nationwide Survey on Malignant Neoplasms in Japan, we calculated the estimated average coverage rates per year between 1969 and 1978 of women aged 30 to 69 years for all of the 3278 municipalities in Japan; we assumed all of the women aged 30 to 69 years were screenees. From all the 3278 municipalities in Japan, 155 municipalities having an estimated average coverage rate of 20% and over were selected as so-called high coverage-rate areas (*A* in Table 1).

From these high coverage-rate areas, we selected 58 municipalities that had age-adjusted rates of PYLL due to uterine cancer in 1969 to 1972 greater than 90% of the average rate of PYLL (230.9 per 100,000 females) of all Japanese (*B* in Table 1).

When high coverage-rate municipalities were limited to the ones with the population size larger than 5000, 93 municipalities were selected (*C* in Table 1). Thirty-six municipalities were selected that had the average coverage rate of 20% and over. The age-adjusted rate of PYLL due to uterine cancer in 1969 to 1972 was greater than 90% of that of Japan having a population larger than 5000 (*D* in Table 1).

Selection of the Control Areas

In order to keep good comparability, two municipalities were selected as controls. These corresponded to each high coverage-rate municipality from those in the same prefecture. These municipalities were matched by population size, coverage rate of the national health insurance, and age-adjusted rate of PYLL due to uterine cancer in 1969 to 1972.

Table 1. Selection of high coverage-rate areas for uterine cancer mass screening.

	Number of high coverage-rate municipalities	Conditions of selection	
A	155	Estimated coverage rate[a]	> 20%
B	58	Estimated coverage rate[a] PYLL in 1969–1972[b]	> 20% > 90% of the average[c] PYLL of all Japan
C	93	Estimated coverage rate[a] Population	> 20% > 5000
D	36	Estimated coverage rate[a] Population PYLL in 1969–1972[b]	> 20% > 5000 > 90% of the average[c] PYLL of all Japan

[a] Estimated average coverage-rate per year in 1969 to 1978 of women aged 30 to 69 years.
[b] The age-adjusted rate of PYLL (potential years of life lost) per 100,000 females from uterine cancer in 1969 to 1972.
[c] The average age-adjusted rate of PYLL from uterine cancer in Japan between 1969 and 1972 was 230.9/100,000 females.

Methods of Matching

We calculated a kind of distance (S) from each high coverage-rate municipality to the all other municipalities in the same prefecture, using community variates as the following formula:

$$S = \sqrt{W_1 \frac{(X_1 - X_{01})^2}{\mathrm{SD}_1^2} + W_2 \frac{(X_2 - X_{02})^2}{\mathrm{SD}_2^2} + W_3 \frac{(X_3 - X_{03})^2}{\mathrm{SD}_3^2}}$$

where the first term of the right-hand side of this formula is the one concerned with age-adjusted rate of PYLL due to uterine cancer in 1969–1972. The second term is the one concerned with population size, and the third term is the one concerned with coverage-rate of the national health insurance, a socio-occupational index. Three values, X_{01}, X_{02}, and X_{03}, denote values of the high coverage-rate municipality, and X_1, X_2 and X_3 denote values of the candidate municipality as control; SD_1, SD_2 and SD_3 denote standard deviations for all municipalities in Japan; and W_1, W_2 and W_3 denote weights proportional to the F-values for partial regression coefficients in the multiple regression analysis, where change of the rate of PYLL due to uterine cancer was regressed on these three most important adjusting factors.

Assuming that the municipality with the minimum distance (S) from each high coverage-rate municipality is the best matched control municipality, two municipalities with the smallest and the second smallest distance (S) were selected as controls.

95% Confidence Interval of the Change in PYLL

Based on the vital statistics from the Ministry of Health and Welfare, we calculated the age-adjusted rates of PYLL due to uterine cancer between 1969 and 1972 and between 1973 and 1977 and their changes by municipality across Japan.

A general method for interval estimation is to assume that some transform of the parameter follows a normal distribution (*9*). For the present study, the logarithmic transformation of the ratio of PYLL was used. Let $Z = \log(r_2/r_1)$ where r_2 is the age-adjusted rate of PYLL in 1973 to 1977, and r_1 is the one in 1969 to 1972. Then

$$V = \mathrm{Var}(z) = \sum_{j=1}^{2} [\textstyle\sum a_i^2 N_i^2 \pi_{ji}(1 - \pi_{ji})/n_{ji}]/(\hat{r}_j^2 N^2)$$

$$\mathrm{CL1}, \mathrm{CLu}(r_2/r_1 - 1) = \exp(Z_0 \pm 1.96\sqrt{V}) - 1$$

CL1 and CLu are the lower/upper confidence limits.

Results

To evaluate the effectiveness of mass screening for uterine cancer, we compared the changes in the age-adjusted rates of PYLL due to uterine cancer from 1969 to 1972 and from 1973 to 1977 between the overall high coverage-rate areas and the overall comparable control areas.

In the 155 high coverage-rate (20% and over) areas (*A* in Table 1), the percent reduction of the average age-adjusted rate of PYLL due to uterine cancer (34.6%) was greater than that (22.3%) in the 310 control areas (statistically not significant at the 5% level). The years of life saved per 100,000 females was 69.6 person-years in the high coverage-rate areas, and greater than that (48.5 person-years) in the control areas (Table 2). The screening rate for uterine cancer was 25.4% among high coverage-rate areas and 9.1% among control areas. The changes in age-specific death rate, the changes in PYLL, and the percent changes in PYLL by 5-year age groups from cancer of the uterus from 1969–1972 to 1973–1977 among the high coverage-rate areas were compared with those among the control areas. Generally speaking, the years of life saved per 100,000 females and the percent reduction in PYLL were greater in the high coverage-rate areas than in the control areas, especially in younger age groups (Table 3).

When the high coverage-rate areas were limited to those with the age-adjusted rate of PYLL due to the uterine cancer in 1969–1972 were greater than 90% of the average rate of PYLL of all Japan (Table 1), the years of life saved and the percent decrease in the average age-adjusted rate of PYLL from cancer of the uterus were also greater in these high coverage-rate areas (271.9 person-years and 69.9%) than in the control areas (125.4 person-years and 39.5%) ($p < 0.05$) (Table 4). The average coverage-rate of uterine cancer screening for high coverage-rate areas was 25.2% and that of the control areas was 8.7%. The years of life saved per 100,000 females and the percent decrease in PYLL by 5-year age groups were generally greater in the high coverage-rate areas than in the control areas, especially in younger age groups (Table 5).

When the high coverage-rate areas were limited to municipalities with the population size larger than 5000 (Table 1) in order to reduce the random variation of rate of PYLL due to small size of population, the similar trends were observed (Tables 6 and 7).

Discussion

Randomized controlled trial is considered to be the most accurate or most convincing method to evaluate the effectiveness of mass screening for cancer because it is free of some biases, such as self-selection bias, lead-time bias, and length bias. Individual allocation method was used in the Health Insurance Plan of Greater New York (HIP) study for breast cancer screening (*10*) or the Mayo Lung Project for lung cancer screening (*11*). Group/areas allocation method was used in Swedish study on mass screening for breast cancer (*12*).

It is difficult to conduct these trials, as shown by the fact that only a few randomized trials for cancer screening have been conducted throughout the world. In Japan, no randomized trials of mass screening for any cancer have been conducted. Consequently, the effectiveness of mass screening for cancer in Japan has been studied by several alternative methods of a randomized trial, i.e., observational studies [time trend analysis (*13–15*)], or case-control studies (*16*). There have been a few studies on the effectiveness of uterine cancer screening in Japan. We tried to compare the trends in the age-adjusted mortality rate from cancer of the uterus for municipalities with intensively screened women (so-called high coverage-rate areas) with those for matched control municipalities (*2–4*).

The final objective of cancer control is to prevent cancer, but currently it seems impossible to completely eliminate cancer as a cause of death. Our attainable objective of mass screening for cancer as a secondary prevention is to prevent or delay cancer mortality and decrease the life shortening due to cancer. As we progress toward this objective, we will gradually shift the age-specific death rate curves to the right (older side). Therefore, we should evaluate screening programs on the basis of whether they decrease the age-specific mortality rates, especially at younger ages, and increase the life expectancy. In the present paper, using the PYLL we also attempted to see whether or not mass screening programs for uterine cancer in Japan could

Table 2. Comparisons of the age-adjusted rates of potential years of life lost (PYLL) due to uterine cancer and their changes between the high coverage-rate areas (*A* in Table 1) and the control areas.

Coverage rate[a]	Number of municipalities	Coverage rate of screening 1969–78, %[b]	Age-adjusted rate of PYLL per 100,000 females 1969–72	1973–77	Years of life lost	Change in PYLL, %[c]	95% confidence interval, %
H	155	25.4	201.1	131.5	−69.6	−34.6	−46.4/−20.3
C	310	9.1	217.6	169.1	−48.5	−22.3	−28.8/−15.2

[a] H, high coverage rate areas; C, control areas.
[b] Average weighted by females aged 30 to 69 years.
[c] Change = $[(r_2 - r_1)/r_1] \times 100\%$; r_1, age-adjusted rate of PYLL due to uterine cancer in 1969–72; r_2, age-adjusted rate of PYLL due to uterine cancer in 1973–77.

Table 3. Comparisons of the age-specific, age-adjusted death rates, change in PYLL from uterine cancer and their changes between the high coverage-rate areas (*A* in Table 1) and the control areas.

Age groups	High coverage-rate areas (155 municipalities) Death rate per 100,000 women 1969–72	1973–77	Difference in death rate	Difference in PYLL[a]	% Change in PYLL	Control areas (310 municipalities) Death rate per 100,000 women 1969–72	1973–77	Difference in death rate	Difference in PYLL[a]	% Change in PYLL
25–29	1.67	0.60	− 1.07	− 53.84	−64.3	1.07	1.00	− 0.07	− 3.8	− 7.0
30–34	4.93	0.68	− 4.25	−192.50	−86.2	1.89	1.90	0.01	0.4	0.5
35–39	2.37	1.15	− 1.22	− 49.28	−51.4	5.41	3.43	− 1.98	− 80.4	−36.7
40–44	4.03	3.41	− 0.61	− 21.91	−15.2	10.83	6.62	− 4.21	−150.5	−38.9
45–49	22.21	9.88	−12.33	−384.13	−55.5	15.98	14.57	− 1.42	− 44.1	− 8.9
50–54	26.08	15.92	−10.16	−270.72	−39.0	26.17	20.02	− 6.15	−163.8	−23.5
55–59	30.16	25.67	− 4.49	−100.12	−14.9	32.26	23.15	− 9.10	−202.9	−28.2
60–64	36.85	29.20	− 7.65	−138.50	−20.8	46.78	34.83	−11.95	−216.3	−25.6
65–69	47.40	34.88	−12.52	−177.83	−26.4	48.93	40.97	− 7.96	−113.0	−16.3
70–74	46.19	49.11	2.92	31.22	6.3	62.69	50.70	−11.99	−128.2	−19.1
75–79	60.76	46.58	−14.18	−109.46	−23.3	69.20	71.56	2.36	18.2	3.4
80–84	58.94	40.11	−18.83	−102.65	−32.0	54.72	68.80	14.08	76.7	25.7
Age-adjusted rate										
30–69[b]	18.55	12.36	− 6.19	−168.2		19.67	14.80	− 4.87	−112.1	
All ages	9.48	6.84	− 2.64	− 69.6		10.58	8.52	− 2.06	− 48.5	
Average coverage-rate of screening[c]			25.4%					9.1%		

[a] Potential years of life lost (PYLL)/100,000 women.
[b] Truncated age-adjusted rate/100,000 women from uterine cancer which is standardized on the age distribution of the Segi-Doll's world population.
[c] Estimated average coverage-rate/year between 1969 and 1978 of women aged 30 to 69 years.

Table 4. Comparisons of the age-adjusted rates of potential years of life lost (PYLL) due to uterine cancer and their changes between the high coverage-rate areas (*B* in Table 1) and the control areas.

Coverage rate[a]	Number of municipalities	Coverage rate of screening 1969–78, %[b]	Age-adjusted rate of PYLL per 100,000 females 1969–72	1973–77	Years of life lost	Change in PYLL, %[c]	95% confidence interval, %
H	58	25.2	388.8	116.9	−271.9	−69.9	−77.4/−60.0
C	116	8.7	317.3	191.9	−125.4	−39.5	−45.5/−32.9

[a] H, high coverage rate areas; C, control areas.
[b] Average weighted by females aged 30 to 69 years.
[c] Change = $[(r_2 - r_1)/r_1] \times 100\%$; r_1, age-adjusted rate of PYLL due to uterine cancer in 1969–72; r_2, age-adjusted rate of PYLL due to uterine cancer in 1973–77.

contribute to the delay of death from this cancer or to the increase of life expectancy, which tend to emphasize reduction in cancer mortality in younger age groups.

Generally speaking, higher coverage rates of mass screening tended to be observed in municipalities with small population size. In the present study, the municipalities with high coverage rates of screening also had relatively small population sizes, and hence the so-called regression toward the mean phenomena may occur because of the random variation of rate of PYLL due to uterine cancer and also because of the small size of population. So, the higher the rate of PYLL in the former period, the steeper it may tend to decrease. This is the reason why the rate of PYLL from uterine cancer in the former period (in 1969 to 1972) should be matched. In addition, other factors such as population size and coverage rate of the national health insurance should also be matched from the aspects of the medical service, industrial structure, and other factors. We selected control municipalities from the same prefecture of corresponding high coverage-rate municipalities to secure the similarity of natural, geographical, or social environment.

The previously mentioned high coverage-rate areas (*A* or *C* in Table 1) may have included a large number of municipalities that have relatively low rates of PYLL due to uterine cancer between 1969 and 1972. The low rates could be partly due to the effects of previous mass screening for uterine cancer and partly due to random variation of rates of PYLL because of the small population in these relevant municipalities.

If these concomitant effects were excluded, we could clarify the effectiveness of mass screening for uterine cancer. Thus, we tried to limit our study to only the municipalities with the age-adjusted rates of PYLL from uterine cancer between 1969 and 1972. These mu-

Table 5. Comparisons of the age-specific, age-adjusted death rates, change in PYLL from uterine cancer and their changes between the high coverage-rate areas (*B* in Table 1) and the control areas.

	High coverage-rate areas (58 municipalities)					Control areas (116 municipalities)				
	Death rate per 100,000 women					Death rate per 100,000 women				
Age groups	1969–72	1973–77	Difference in death rate	Difference in PYLL[a]	% Change in PYLL	1969–72	1973–77	Difference in death rate	Difference in PYLL[a]	% Change in PYLL
25–29	4.41	0.00	− 4.41	−220.8	−100.0	1.81	1.02	− 0.78	− 39.2	−43.3
30–34	13.24	0.00	−13.24	−599.6	−100.0	2.77	1.43	− 1.35	− 61.0	−48.6
35–39	6.31	1.53	− 4.78	−193.5	− 75.7	8.65	3.80	− 4.85	−196.5	−56.1
40–44	4.73	1.31	− 3.42	−122.3	− 72.3	16.83	7.86	− 8.98	−321.2	−53.3
45–49	41.12	9.03	−32.09	−999.7	− 78.1	24.67	17.18	− 7.49	−233.3	−30.4
50–54	56.97	19.91	−37.06	−987.3	− 65.1	38.94	22.78	−16.16	−430.4	−41.5
55–59	55.40	27.35	−28.06	−625.1	− 50.6	47.65	27.43	−20.22	−450.5	−42.4
60–64	75.36	22.26	−53.09	−961.0	− 70.5	64.87	40.15	−24.72	−447.5	−38.1
65–69	69.19	15.57	−53.62	−761.4	− 77.5	65.63	48.62	−17.01	−241.5	−25.9
70–74	57.50	65.77	8.27	88.5	14.4	83.02	48.21	−34.80	−372.0	−41.9
75–79	117.56	46.35	−71.21	−549.8	− 60.6	83.56	78.29	− 5.27	− 40.7	− 6.3
80–84	62.16	49.37	−12.80	− 69.8	− 20.6	54.85	72.65	17.80	97.0	32.5
Age-adjusted rate										
30–69[b]	35.20	10.40	−24.80	−626.4		28.98	17.79	−11.19	−283.5	
All ages	17.17	6.37	−10.80	−271.9		14.87	9.57	− 5.30	−125.4	
Average coverage-rate of screening[c]			25.2%					8.7%		

[a] Potential years of life lost (PYLL)/100,000 women.
[b] Truncated age-adjusted rate/100,000 women from uterine cancer which is standardized on the age distribution of the Segi-Doll's world population.
[c] Estimated average coverage rate/year between 1969 and 1978 of women aged 30 to 69 years.

Table 6. Comparisons of the age-adjusted rates of potential years of life lost (PYLL) due to uterine cancer and their changes between the high coverage-rate areas (*C* in Table 1) and the control areas.

Coverage rate[a]	Number of municipalities	Coverage rate of screening 1969–78, %[b]	Age-adjusted rate of PYLL per 100,000 females 1969–72	1973–77	Years of life lost	Change in PYLL, %[c]	95% confidence interval, %
H	93	25.0	204.2	128.1	−76.1	−37.3	−49.5/−22.0
C	186	9.1	208.1	160.4	−47.7	−22.9	−30.7/−14.2

[a] H, high coverage rate areas; C, control areas.
[b] Average weighted by females aged 30 to 69 years.
[c] Change = $[(r_2 - r_1)/r_1] \times 100\%$; r_1, age-adjusted rate of PYLL due to uterine cancer in 1969–72; r_2, age-adjusted rate of PYLL due to uterine cancer in 1973–77.

Table 7. Comparisons of the age-adjusted rates of potential years of life lost (PYLL) due to uterine cancer and their changes between the high coverage-rate areas (*D* in Table 1) and the control areas.

Coverage rate[a]	Number of municipalities	Coverage rate of screening 1969–78, %[b]	Age-adjusted rate of PYLL per 100,000 females 1969–72	1973–77	Years of life lost	Change in PYLL, %[c]	95% confidence interval, %
H	36	25.0	367.6	125.4	−242.1	−65.9	−75.1/−53.1
C	72	9.0	295.0	178.8	−116.2	−39.4	−47.0/−30.6

[a] H, high coverage rate areas; C, control areas.
[b] Average weighted by females aged 30 to 69 years.
[c] Change = $[(r_2 - r_1)/r_1] \times 100\%$; r_1, age-adjusted rate of PYLL due to uterine cancer in 1969–72; r_2, age-adjusted rate of PYLL due to uterine cancer in 1973–77.

nicipalities had rates greater than 90% of the average rate of PYLL (230.9 person-years per 100,000 women) of all Japan (*B* or *D* in Table 1). This 90% level, although somewhat arbitrary, was used to include adequate numbers of municipalities in the analysis. These analyses demonstrated a significant reduction of PYLL due to uterine cancer in high coverage-rate areas. Factors other than mass screening, such as the decrease in the incidence from uterine cancer might contribute to the reduction in PYLL, but such data were not available. So we could not definitely claim a reduction of PYLL, but these results suggested that mass screening programs for uterine cancer may be possible to save the years of life because of this cancer.

The PYLL tends to lay weight on the reduction in cancer mortality in younger age groups. Mass screening programs for cancer should be able to prevent or delay cancer deaths, and then to increase life expectancy. From the present study, it was suggested the PYLL was one of the appropriate indices in evaluating the impact of mass screening for cancer.

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